

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Dean L. Engelhardt et al. Group Art Unit: 1807
Serial No. 08/046,004 Examiner: Not Yet Known
Filed: April 9, 1993 Prev. Exm'r: Amelia Yarbrough
Title: PHOSPHATE-MOIETY LABELED NUCLEOTIDES

INFORMATION DISCLOSURE STATEMENT

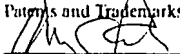
HON. COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

Sir:

This Information Disclosure Statement is filed in accordance with 37 C.F.R. §§1.56 and 1.97-1.98. The items listed on Form PTO-1449, a copy of which is enclosed, may be deemed to be pertinent to the above-identified application and are made of record to assist the Patent and Trademark Office in its examination of this application. The Examiner is respectfully requested to fully consider the items and to independently ascertain their teaching.

1. ☒ For each of the following items listed on the enclosed copy of Form PTO-1449 that is not in the English language, an English language translation of that item or a portion thereof or a concise explanation of the relevance of that item is enclosed: Exhibits 34-36, 66-67, 69, 100-102
2. ☐ For each of the following items listed on the enclosed copy of form PTO-1449 that is not in the English language, a concise explanation of the relevance of that item is incorporated in the specification of the above-identified application.
3. ☐ Any copy of the items on the enclosed copy of Form PTO-1449 that is not enclosed with this Information Disclosure Statement was previously cited by or submitted to the Patent and Trademark Office in the prior ☐ Divisional or ☐ Continuation-In-Part application under 37 C.F.R. §1.60, U.S. Serial No. _____, filed _____.
4. ☐ No fee is due under 37 C.F.R. §1.17(p) for this Information Disclosure Statement since it is being filed in compliance with:
 - ☐ 37 C.F.R. §1.97(b)(1), within three months of the filing date of the above-identified application.
 - ☐ 37 C.F.R. §1.97(b)(2), within three months of the date of entry into the national stage as set forth in §1.491 in an international application.
 - ☐ 37 C.F.R. §1.97(b)(3), before the mailing ~~date of a first Office action~~ on the merits.

Enz-5 (D6)(C1)

EXPRESS MAIL CERTIFICATE	
"Express Mail" Label No	EF971126539
Deposit Date	AUGUST 22, 1994
I hereby certify that this paper and the attachments herein are being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to the Commissioner of Patents and Trademarks, Washington DC 20231	
 Ronald C. Fedus	August 22, 1994 Date

Dean L. Engelhardt et al.

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Filed: April 9, 1993

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Under 37 C.F.R. §§1.56 & 1.97-1.98 - August 22, 1994)

5. ☐ No fee is due under 37 C.F.R. §1.17(p) for this Information Disclosure Statement since it is being filed in compliance with 37 C.F.R. §1.97(c), after the period specified in paragraph 4 above but before the mailing date of a final action or a Notice of Allowance (where there has been no prior final action), and is accompanied by one of the certifications pursuant to 37 C.F.R. §1.97(e) set forth in paragraph 9 below.
6. ☒ A fee is due under 37 C.F.R. §1.17(p) for this Information Disclosure Statement since it is being filed in compliance with 37 C.F.R. §1.97(c), after the period specified in paragraph 4 above but before the mailing date of a final action or a notice of allowance (where there has been no prior final action):
- ☐ A check in the amount of \$200.00 is enclosed in payment of the fee.
- ☒ Charge the fee to Deposit Account No. 05-1135, Order No. ENZ-5 (D6)(C1). A DUPLICATE COPY OF THIS SHEET IS ATTACHED.
7. ☐ A fee is due under 37 C.F.R. §1.17(i)(1) for this Information Disclosure Statement since it is being filed in compliance with 37 C.F.R. §1.97(d), after the mailing date of a final action or a notice of allowance, whichever comes first, but before payment of the issue fee, and is accompanied by:
- a. one of the certification pursuant to 37 C.F.R. §1.97(e) set forth in paragraph 9 below; and
- b. the attached petition requesting consideration of this Information Disclosure Statement; and
- c. the fee due under 37 C.F.R. §1.17(i)(1) which is paid as set forth in paragraph 10 below.
8. ☐ A fee is due under 37 C.F.R. §1.17(i)(1) for this Information Disclosure Statement since it is being filed in compliance with:
- a. ☐ 37 C.F.R. §1.313(b)(3), after the issue fee has been paid and information cited in this Information Disclosure Statement may render at least one claim unpatentable and is accompanied by the attached Petition To Withdraw Application From Issue;
- b. ☐ 37 C.F.R. §1.313(b)(5), after the issue fee has been paid and information cited in this Information Disclosure Statement is to be considered in a Continuation application upon abandonment of the instant application and is accompanied by the attached Petition To Withdraw Application From Issue.
- c. ☐ The fee due under 37 C.F.R. §1.17(i)(1) is paid as set forth in paragraph 10 below.

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Under 37 C.F.R. §§1.56 & 1.97-1.98 - August 22, 1994)

9. ☐ I hereby certify that each item of information contained in this Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this Information Disclosure Statement.

☐ I hereby certify that no item of information in the Information Disclosure Statement filed herewith was cited in a communication from a foreign patent office in a counterpart foreign application or, to my knowledge after making reasonable inquiry, was known to any individual designated in §1.56(c) more than three months prior to the filing of this Information Disclosure Statement.

10. ☐ A check in the amount of \$130.00 is enclosed in payment of the fee due under 37 C.F.R. §1.17(i)(1).

☐ Charge the fee under 37 C.F.R. §1.17(i)(1) to Deposit Account No. 05-1135. Order No. _____. A DUPLICATE COPY OF THIS SHEET IS ATTACHED.

☒ The Commissioner is hereby authorized to charge any additional fees which may be required for this Information Disclosure Statement, or credit any overpayment to Deposit Account No. 05-1135. A DUPLICATE COPY OF THIS SHEET IS ATTACHED.

Respectfully submitted,

Dated: August 22, 1994

By: _____

RONALD C. FEDUS

Registration No. 32,567

Mailing Address:

ENZO DIAGNOSTICS, INC.
c/o Enzo Biochem, Inc.
575 Fifth Avenue
New York, New York 10017
Telephone: (212) 856-0876

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Dean L. Engelhardt et al.)	
Serial No.	08/046,004)	Group Art Unit: 1807
Filed:	April 9, 1993)	Examiner: Not Yet Known
Title:	PHOSPHATE-MOIETY LABELED NUCLEOTIDES)	Prev. Ex'r: Amelia Yarbrough, Ph.D.

575 Fifth Avenue, 18th Floor
New York, New York 10017
August 22, 1994

FILED BY EXPRESS MAIL

Hon. Commissioner of Patents and Trademarks
Washington, D.C. 20231

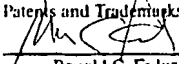
**INFORMATION DISCLOSURE
STATEMENT UNDER 37 C.F.R. §§1.56 & 1.97-1.98**

Dear Sirs:

Pursuant to the provisions of 37 C.F.R. §§1.97-1.98, and in full compliance with their duty of disclosure under 37 C.F.R. §1.56, Applicants, through their attorney, are bringing the following one hundred and two (102) documents to the attention of the U.S. Patent and Trademark Office and the Examiner handling their above-identified application:

1. Becker et al., "Irreversible Inhibition of Biotin Transport in Yeast by Biotinyl-p-nitrophenyl Ester," Proc. Nat'l. Acad. Sci. (USA) 68:2604-2607 (1971)¹ [Exhibit 1];
2. Halloran et al., "The Preparation of Nucleotide-protein Conjugates: Carbodiimides as Coupling Agents," J. Immunol., 96(3):373-378 (1966)¹ [Exhibit 2];
3. Manning et al., "A New Method of in situ Hybridization," Chromosoma, 53:107-117 (1975)¹ [Exhibit 3];
4. Kropinski et al., Gen. Virol., 6:85 (1970)^{1, 5} [Exhibit 4];

Enz-5 (D6)(C1)

EXPRESS MAIL CERTIFICATE	
"Express Mail" Label No.	EF971126539
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 Ronald C. Fedus	AUGUST 22, 1994 Date

5. Kropinski et al., "5-(4-Aminobutylaminomethyl) uracil, an Unusual Pyrimidine from the Deoxyribonucleic Acid of Bacteriophage ϕ W-14," Biochemistry, 12(1):151-157 (1973)¹ [Exhibit 5];
6. Bhat, Syn. Proc. in Nucleic Acid Chem., Vol. I., p. 521 (1968)^{1, 5} [Exhibit 6];
7. Torrence et al., "5-O-Alkylated Derivatives of 5-Hydroxy-2'-deoxyuridine as Potential Antiviral Agents. Anti-Herpes Activity of 5-Propynyloxy-2'-deoxyuridine," J. Med. Chem., 21(2):228-231 (1978)¹ [Exhibit 7];
8. Michelson, "Synthesis Of Nucleotide Anhydrides By Anion Exchange," Biochem. Biophys. Acta., 91:1-13 (1964)¹ [Exhibit 8];
9. Cech et al. "A facile synthesis of 5-(perfluoroalkyl)-pyrimidines," Nucl. Acids Res., 2(11):2183-2192 (1979)¹ [Exhibit 9];
10. Schram et al., "Pyrrolopyrimidine Nucleosides VIII. Synthesis of Sangivamycin Derivatives Possessing Exocyclic Heterocycles at C5," J. Carbohydrate, Nucleosides, Nucleotides, 1(1):39-54 (1974)¹ [Exhibit 10];
11. Bleackley et al., "The preparation of 5-cyanouracil and 5-cyano-2'-deoxyuridine from the corresponding 5-iodo derivative and cuprous cyanide," Nucl. Acids Res., 2(5):683-690 (1975)¹ [Exhibit 11];
12. Roberts et al., "Uridine and Cytidine Derivatives," J. Am. Chem. Soc. 74:668-669 (1952)¹ [Exhibit 12];
13. Bauman et al., "Rapid and High Resolution Detection of in situ Hybridisation to Polytene Chromosomes Using Fluorochrome-labeled RNA," Chromosoma, 84:1-18 (1982)¹ [Exhibit 13];
14. Bauman et al., "A new method for fluorescence microscopical localization of specific DNA sequences by in situ hybridization of fluorochrome-labelled RNA," Exp. Cell Res., 128:485-490 (1980)¹ [Exhibit 14];

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Under 37 C.F.R. §§ 1.56 & 1.97-1.98 - August 22, 1994)

15. Gerhard et al., "Localization of a Unique Gene by Direct Hybridization in situ," Proc. Natl. Acad. Sci. (USA), 78(6):3755-3759 (1981)¹ [Exhibit 15];
16. Miller, J., "Experiment 52, Assay of the lac Repressor by Binding to Operator," Experiments in Molecular Genetics, Cold Spring Harbor Laboratory pp. 367-370 (1972)¹ [Exhibit 16];
17. Ueda et al., "Conversion of Uridine Nucleotides to the 6-Cyano Derivatives: Synthesis of Orotidylic Acid (Nucleosides and Nucleotides)," J. Carbohydr. Nucleosides, Nucleotides, 5(3):261-271 (1978)¹ [Exhibit 17];
18. Brunngraber et al., "Purification and Properties of a Nucleoside Phosphotransferase from Carrot," J. Biol. Chem., 242:4834-4840 (1967)¹ [Exhibit 18];
19. Wilchek et al., "Modification of the Carboxyl Groups of Ribonuclease by Attachment of Glycine or Alanylglycine," Biochemistry, 6(1):247-252 (1967)¹ [Exhibit 19];
20. Vogt, "Purification and Properties of S₁ Nuclease from *Aspergillus*," Methods in Enzymology, 65:248-255 (1980)¹ [Exhibit 20];
21. Ward et al., U.S. Patent No. 4,711,955, issued Dec. 8, 1987, which patent is a continuation of U.S. Patent Application Serial No. 255,223, filed April 17, 1981 and abandoned¹ [Exhibit 21];
22. Monod et al., "On the Nature of Allosteric Transitions: A Plausible Model," J. Mol. Biol., 12:88-118 (1965)¹ [Exhibit 22];
23. Pastan et al., "Cyclic Adenosine Monophosphate in Bacteria," Science, 169:339-344 (1969)¹ [Exhibit 23];
24. Gilbert et al., "The Nucleotide Sequence of the lac Operator," Proc. Natl. Acad. Sci. (USA), 70(12):3581-3584 (1973)¹ [Exhibit 24];

25. Pardee, "Membrane Transport Proteins," Science, 162:632-637 (1968)¹
[Exhibit 25];
 26. Hazelbaur et al., "Role of the Galactose Binding Protein in Chemotaxis of Escherichia coli toward Galactose," Nature New Bio., 230:101-104 (1971)¹
[Exhibit 26];
 27. Caruthers, Second Annual Congress for Recombinant DNA Research, Los Angeles, CA (1982)^{1, 5} [Exhibit 27];
 28. Stavrianopoulos, U.S. Patent No. 4,707,440 issued November 17, 1987^{2, 7}
[Exhibit 28];
 29. Robins et al., U.S. Patent No. 4,038,480 issued July 26, 1977^{2, 7, 8}
[Exhibit 29];
 30. Carrico et al., U.S. Patent No. 4,213,893 issued July 22, 1980^{2, 7, 8, 23}
[Exhibit 30];
 31. Carrico et al., U.S. Patent No. 4,255,566 issued March 10, 1981^{2, 4, 7, 8, 21, 23}
[Exhibit 31];
 32. Gohlke et al., U.S. Patent No. 4,378,458 issued March 29, 1983^{2, 7, 8, 19}
[Exhibit 32];
 33. Bückmann, U.S. Patent No. 4,443,594 issued April 17, 1984^{2, 7, 8} [Exhibit 33];
 34. Agency Ind. Sci., Japan Patent No. 53-133283^{2, 8, 26} (Nov. 1934) [Exhibit 34];
 35. Imahori et al., U.K. Patent Application No. GB 2 036 029 A, published June 25, 1980^{2, 8} [Exhibit 35];
 36. Chugai Pharm., Japan Patent No. 57-11999 (Jan. 1982)^{2, 8, 26} [Exhibit 36];
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37. Agency Ind. Sci., Japan Patent No. 60-96610 (May 1985)^{2, 6, 8} [Exhibit 37];
38. Ward et al., European Patent No. 0 063 879 B1 granted November 23, 1989^{2, 4, 8, 14, 15, 16, 18, 19} [Exhibit 38];
39. Carrico et al., U.K. Patent Application No. GB 2 040 943 A published Sept. 3, 1980^{2, 4, 21} [Exhibit 39];
40. Langer et al., "Enzymatic synthesis of biotin-labeled polynucleotides: Novel nucleic acid affinity probes," Proc. Natl. Acad. Sci. (USA), 78(11):6633-6637 (1981)^{2, 4, 9, 18, 22} [Exhibit 40];
41. Nishimura et al., "Synthetic Nucleosides and Nucleotides. XV. 1) 5-Dimethylamino-2-oxidoisoquinolin-1-yl Diazomethane: A Novel Water-Soluble Fluorescent Labelling Agent for Nucleotides," Chem. Pharm. Bull., 28(6):1695-1703 (1980)^{2, 4} [Exhibit 41];
42. Kwah et al., "Myocardial Infarct Imaging of Antibodies to Canine Cardiac Myosin with Indium-111-Diethylenetriamine Pentaacetic Acid," Science 209:295-297 (1980)³ [Exhibit 42];
43. Benovic et al., U.S. Patent No. 4,460,772 issued July 17, 1984⁸ [Exhibit 43];
44. Torrence et al., "Interferon Inducers: General Survey and Classification," Methods in Enzymology, Vol. 78, Interferons, Part A, pp. 291-299 (Pestka, Edu.), Academic Press, New York, 1981¹⁰ [Exhibit 44];
45. Harnden, U.S. Patent No. 3,931,397 issued January 6, 1976¹¹ [Exhibit 45] ;
46. Lampson et al., U.S. Patent No. 4,124,702 issued November 7, 1978¹¹ [Exhibit 46] ;
47. Arimura et al., U.S. Patent No. 4,313,938 issued February 2, 1982¹¹ [Exhibit 47] ;

48. Ward et al., U.S. Patent No. 4,711,955 issued Dec. 8, 1987^{9, 12, 15, 18, 22, 24}
[Exhibit 48];
49. Falkow et al., U.S. Patent No. 4,358,535 issued Nov. 9, 1982^{12, 14, 15, 16, 17, 24}
[Exhibit 49];
50. Engelhardt et al., U.S. Patent No. 5,260,433, issued on November 9, 1993¹³
[Exhibit 50];
51. Kourilsky et al., United Kingdom Patent Application No. GB 2 019 408 A
published October 31, 1979^{14, 16} [Exhibit 51];
52. Kourilsky et al., U.S. Patent No. 4,581,333 issued April 8, 1986¹⁶ [Exhibit
52];
53. Siebenlist et al., "Contacts between Escherichia coli RNA polymerase and an
early promoter of phage T7," Proc. Natl. Acad. Sci. (USA), 77(1):122-126,
January 1980¹⁷ [Exhibit 53];
54. Maxam et al., "A New Method for Sequencing DNA," Proc. Natl. Acad. Sci.
(USA), 74(2):560-564, 1977¹⁷ [Exhibit 54];
55. Heggeness et al., "Avidin Binds To Condensed Chromatin," Stain Technol.
52(3):165-169 (1977)¹⁸ [Exhibit 55];
56. Heggeness et al., "Use of the Avidin-Biotin Complex For the Localization of
Actin and Myosin with Fluorescence Microscopy," J. Cell Biol. 73:783-788
(1977)¹⁸ [Exhibit 56];
57. Bayer et al., "The Use of the Avidin-Biotin Complex as a Tool in Molecular
Biology," Methods of Biochem Analysis 26:1-45 (1980)¹⁸ [Exhibit 57];
58. Hoffman et al., "Iminobiotin affinity columns and their application to retrieval
of streptavidin," Proc. Natl. Acad. Sci. 77(8) :4666-4668 (1980)¹⁸ [Exhibit
58];

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59. Pardue et al., "Nucleic Acid Hybridization to the DNA of Cytological Preparations," Methods in Cell Biol. 10:1-16 (1975)¹⁸ [Exhibit 59];
60. Bergstrom et al., "C-5 Substituted Pyrimidine Nucleosides. 2. Synthesis via Olefin Coupling to Organopalladium Intermediates Derived from Uridine and 2'-Deoxyuridine," JACS 100:8106-8112 (1978)¹⁸ [Exhibit 60];
61. Bigge et al., "Palladium-Catalyzed Coupling Reactions of Uracil Nucleosides and Nucleotides," JACS 102:2033-2038 (1979)¹⁸ [Exhibit 61];
62. Rigby et al., "Labeling Deoxyribonucleic Acid to High Specific Activity in Vitro by Nick Translation with DNA Polymerase I," J. Mol. Biol. 113:237-251 (1977)¹⁸ [Exhibit 62];
63. Bourguignon et al., "DNA of Minute Virus of Mice:Self-Priming, Nonpermuted Single-Stranded Genome with a 5'-Terminal Hairpin Duplex," J. Virol. 20:290-306 (1976)¹⁸ [Exhibit 63];
64. Miller et al., "A general method for permeabilizing mono-layer and suspension cultured animal cells," Exp. Cell Res. 120:421-425 (1979)¹⁸ [Exhibit 64];
65. Miyoshi et al., U.S. Patent No. 4,605,735 issued August 12, 1986¹⁹ [Exhibit 65];
66. Japan Patent No. 60-169495 issued September 1985^{19, 26} [Exhibit 66];
67. Helene et al., European Patent Application No. 0 169 787 A1 published January 29, 1986^{19, 26} [Exhibit 67];
68. Klevan et al., PCT Patent Application No. WO 86/02929 published May 22, 1986¹⁹ [Exhibit 68];
69. Japan Patent No. 57-42632 issued March 1986^{19, 26} [Exhibit 69];

70. Japan Patent 61-103824 issued May 1986^{19, 26} [Exhibit 70];
71. Suhadolnik et al., U.S. Patent No. 9,708,935 issued November 24, 1987²⁰ [Exhibit 71];
72. Rapaport, U.S. Patent No. 4,880,918 issued November 14, 1989²⁰ [Exhibit 72];
73. Klevan et al., U.S. Patent No. 4,828,979 issued May 9, 1989²⁵ [Exhibit 73];
74. Musso et al., U.S. Patent No. 4,833,251 issued May 23, 1989²⁵ [Exhibit 74];
75. Carrico et al., European Patent No. 0 027 631 B1 granted May 5, 1982²⁵ [Exhibit 75];
76. Urdea et al., European Patent Application No. 0 225 807 A2 published June 16, 1987²⁵ [Exhibit 76];
77. Schulman et al., "Attachment of protein affinity-labeling reagents of variable length and amino acid specificity to E. coli tRNA^{Met}," Nuc. Acid Res., Vol. 9, No. 5 (1981)²⁵ [Exhibit 77];
78. Langer, et al., "Enzymatic synthesis of biotin-labeled polynucleotides: Novel nucleic acid affinity probes," Chemical Abstracts, Vol. 96, No. 7, Feb. 15, 1982, pg. 207, Abstract No. 47771z^{4, 21} [Exhibit 78];
79. Clechet, P. et al., "Trace analysis of barium in water by means of cation resin-loaded paper and x-ray fluorescence analysis," Chemical Abstracts, Vol. 94, No. 25, June 22, 1981, pg. 366, Abstract No. 214298t⁴ [Exhibit 79];
80. Duke et al., "Conformational change accompanying modification of myosin ATPase," Chemical Abstracts, Vol. 66, No. 9, Feb. 27, 1967, pg. 3326, Abstract No. 35045h⁴ [Exhibit 80];

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Page 9 (Information Disclosure Statement

Under 37 C.F.R. §§ 1.56 & 1.97-1.98 - August 22, 1994)

81. Duke et al., "Conformational change accompanying modification of myosin ATPase," Biochem. Biophys. Acta, 126:600-603 (1966)⁴ [Exhibit 81];
82. Secrist, III et al., U.S. Patent No. 3,960,840 issued June 1, 1976^{4, 21} [Exhibit 82];
83. Boguslaski et al., U.S. Patent No. 4,230,797 issued October 28, 1980^{4, 21} [Exhibit 83];
84. Kathawala et al., "Darstellung von Desoxy-oligonucleotiden Mit 2'.3'-[2.4-Dimethoxy-benzyliden]-uridin als Phosphat-Schutzgruppe," Liebigs Ann. Chem., 712:195-200 (1968)⁴ [Exhibit 84];
85. Trouet et al., "Targeting of antitumor and antiprotozoal drugs by covalent linkage to protein carriers," Chemical Abstracts, Vol. 98, No. 9, Feb. 28, 1983, pg. 334-335, Abstract No. 77997m⁴ [Exhibit 85];
86. Trouet et al., "Targeting of antitumor and antiprotozoal drugs by covalent linkage to protein carriers," NATO Adv. Study Inst. of Targeting of Drugs, Series A, Life Sciences, 47:19-30, Plenum Press, New York (1981)⁴ [Exhibit 86];
87. Kourilsky et al., PCT Application No. WO 83/02276 published July 7, 1983^{4, 21} [Exhibit 87];
88. Kourilsky et al., PCT Application No. WO 83/02277 published July 7, 1983^{4, 21} [Exhibit 88];
89. Angerer et al., "An Electron Microscope Study of the Relative Positions of the 4S and Ribosomal RNA Genes In HeLa Cell Mitochondrial DNA," Cell, 9:81-90 (1976)⁴ [Exhibit 89];
90. Scherberg, U.S. Patent No. 4,260,737 issued April 7, 1981⁴ [Exhibit 90];

91. Mackey et al., "Preparation and Characterization of Highly Radioactive in Vitro Labeled Adenovirus DNA and DNA Restriction Fragments," Biochemistry, 16(20):4478-4482 (1977)⁴ [Exhibit 91];
92. Zhenodarova et al., "Spin-labeled Derivatives of Oligoribonucleotides as Spin Probes for Studying the Mechanism of the Effect of Enzymes," Chemical Abstracts, Vol. 91, 1979, pg. 303, Abstract No. 85951n⁴ [Exhibit 92];
93. Institute of Biophysics et al., Soviet Union Patent Application A 659 573, April 30, 1979^{4, 6} [Exhibit 93];
94. Crea, U.S. Patent No. 4,310,662 issued January 12, 1982⁴ [Exhibit 94];
95. Salam et al., "Synthesis of Nucleoside 5'-(β -D-Glucopyranosyl Monophosphates) by the Sugar Ortho Ester Route," Carbohydrate Research, 102:139-146 (1982)⁴ [Exhibit 95];
96. Salam et al., "Synthesis of Acetylated α - and β -L-Fucosyl Esters of Nucleoside 5'-Monophosphates by the Orthoester Route," Nucleosides & Nucleotides, 1(2):155-161 (1982)⁴ [Exhibit 96];
97. Gohlke et al., European Patent Application No. O 061 762 A2 published Oct. 6, 1982⁴ [Exhibit 97];
98. Kang et al., European Patent Application No. O 061 760 A1 published Oct. 6, 1982⁴ [Exhibit 98];
99. Kang, European Patent Application No. O 061 761 A1 published Oct. 6, 1982⁴ [Exhibit 99];
100. Sela et al., German Patent Application No. DE-A-25-07-901, published Sept. 10, 1970^{4, 26} [Exhibit 100];
101. Theurer, German Patent Application No. DE-A-18-14-134, published January 28, 1971^{4, 26} [Exhibit 101]; and

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102. Theurer, German Patent Application No. DE-A-16-17-886, published Sept. 2, 1976^{4, 26} [Exhibit 102].

Of the one hundred and two (102) above-submitted documents, twenty-seven (27) documents (Exhibits 1-27) were cited in the instant specification; fifty-five (55) documents (Exhibits 28-78, 82-83 and 87-88) were cited or made of record in the prosecution of the instant and/or related applications; and thirty (30) documents (Exhibits 31, 38-41 and 78-102) were cited by the European Patent Office in the prosecution of the six (6) corresponding European applications, namely application numbers: 83106112.2 which issued as patent no. 0 097 373 B1, 0 285 057 A2, 0 285 950 A3, 0 302 175 A3, 0 286 898 A3, 0 285 058 A3, published on Oct. 10, 1992, Oct. 5, 1988, Oct. 12, 1988, Feb. 8, 1989, Oct. 19, 1988 and Oct. 5, 1988, respectively.

A completed Form PTO-1449 listing the above-submitted documents is also attached hereto as Exhibit 103.

By this voluntary citation of art, Applicants and their attorney are requesting that the documents be made of record in the instant application.

The above citation of references is not a representation that these documents constitute a complete or exhaustive listing, nor that the above listing necessarily includes the closest or most relevant references, nor are these documents necessarily a complete listing of all references known to Applicants or their attorney. It is simply a voluntary citation of references made in good faith, which is not intended to serve in any way as a substitute for the Examiner's own search.

In view of the general and specific features described and claimed in the present application, Applicants respectfully submit that the present invention is neither suggested nor disclosed by the documents referred to above and is thus patentably distinct thereover.

Applicants do not believe, and do not submit, by the citation of these references, that these references, either by themselves or in combination with other

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Under 37 C.F.R. §§1.56 & 1.97-1.98 - August 22, 1994)

references, render the invention prima facie obvious under the new duty of disclosure rules.

Applicants respectfully request that the Examiner make the above-submitted documents of record in the instant application. Applicants further request that the Examiner consider these documents as any of them may relate to the instant application.

The fee under 37 C.F.R. §1.17(p) for filing this Information Disclosure Statement is \$200.00. The Patent and Trademark Office is hereby authorized to charge the amount of this fee (and any other fees in connection with this IDS) to Deposit Account No. 05-1135, or to credit any overpayment thereto.

Respectfully submitted,



Ronald C. Fedus
Registration No. 32,567
Attorney for Applicants

ENZO DIAGNOSTICS, INC.
c/o Enzo Biochem, Inc.
575 Fifth Avenue, 18th Floor
New York, New York 10017
Tel. (212) 856-0876

Footnotes

1. Cited in the specifications of the following nineteen (19) U.S. Patent Applications:
 - 1) 06/391,440, filed June 23, 1982;
 - 2) 06/674,352 filed November 21, 1984;
 - 3) 07/140,980 filed January 5, 1988;
 - 4) 07/685,982 filed April 15, 1991;
 - 5) 07/957,549 filed October 6, 1992;
 - 6) 07/539,279 filed June 15, 1990;
 - 7) 07/962,381 filed October 16, 1992;
 - 8) 07/097,571 filed September 14, 1987
 - 9) 08/125,492 filed September 28, 1993;
 - 10) 07/532,704 filed June 4, 1990, which application issued as U.S. Patent No. 5,241,060 on August 31, 1993;
 - 11) 07/960,071 filed October 13, 1992;
 - 12) 08/046,004 filed April 9, 1993 (the instant application);

Dean L. Engelhardt et al.

Serial No.: 08/046,004

Filed: April 9, 1993

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Under 37 C.F.R. §§1.56 & 1.97-1.98 - August 22, 1994)

- 13) 07/567,039 filed August 13, 1990, which application issued as U.S. Patent No. 5,260,433 on November 9, 1993;
 - 14) 07/548,348 filed July 2, 1990;
 - 15) 07/954,772 filed September 30, 1992;
 - 16) 07/096,986 filed September 14, 1987;
 - 17) 07/531,953 filed June 1, 1990;
 - 18) 07/532,461 filed May 31, 1990;
 - 19) 07/520,682 filed May 8, 1990.
2. Cited in an Office Action dated September 12, 1991 in connection with the prosecution of U.S. Patent Application Serial No. 07/685, 982 filed April 15, 1991;
 3. Cited in an Office Action dated February 18, 1993 in connection with the prosecution of U.S. Patent Application Serial No. 07/685,982 filed April 15, 1991;
 4. Cited by the European Patent Office.
 5. This document is not available.
 6. An English abstract of this patent or patent application is not available.
 7. Cited in an Office Action dated October 16, 1990 in connection with the prosecution of U.S. Patent Application No. 07/140,980 filed January 5, 1988.
 8. Cited in an Office Action dated February 20, 1986 in connection with the prosecution of U.S. Patent Application No. 06/674,352 filed November 21, 1984.
 9. Cited in an Office Action dated December 13, 1993 in connection with the prosecution of U.S. Patent Application No. 08/125,492 filed September 28, 1993.
 10. Cited in an Office Action dated October 13, 1989 in connection with the prosecution of U.S. Parent Application No. 07/097,571 filed September 14, 1987.
 11. Cited in an Office Action dated July 1, 1993 in connection with the prosecution of U.S. Patent Application No. 07/962,381 filed October 16, 1992.
 12. Cited in an Office Action dated October 1, 1991 in connection with the prosecution of U.S. Patent Application No. 07/532,704 filed June 4, 1990, which application issued as U.S. Patent No. 5,241,060 on August 31, 1993.
 13. Cited in an Office Action dated January 10, 1994 in connection with the prosecution of U.S. Patent Application No. 07/960,071 filed October 13, 1992.
 14. Cited in an Office Action dated October 30, 1991 in connection with the prosecution of U.S. Patent Application No. 07/567,039 filed August 13, 1990, which issued as U.S. Patent No. 5,260,433 on November 9, 1993.

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15. Cited in an Office Action dated September 30, 1992 in connection with the prosecution of U.S. Patent Application No. 07/954,772 filed September 30, 1992.
16. Cited in an Office Action dated September 25, 1991 in connection with the prosecution of U.S. Patent Application No. 07/548,348 filed July 2, 1990.
17. Cited in an Office Action dated June 3, 1992 in connection with the prosecution of U.S. Patent Application No. 07/954,772 filed September 30, 1992.
18. Cited in an Office Action dated November 25, 1991 and in an Information Disclosure Statement Under 37 C.F.R. §§1.56 and 1.99 filed August 19, 1991 in connection with U.S. Patent Application No. 07/539,279 filed June 15, 1990.
19. Cited in an Office Action dated July 20, 1988 in connection with the prosecution of U.S. Patent Application No. 07/096,986 filed September 14, 1987.
20. Cited in an Office Action dated February 14, 1991 in connection with the prosecution of U.S. Patent Application No. 07/096,986, filed September 14, 1987.
21. Cited in an Information Disclosure Statement Under 37 C.F.R. §§ 1.56 and 1.99 filed February 13, 1992 in connection with the prosecution of U.S. Patent Application No. 07/096,986, filed September 14, 1987.
22. Cited in an Office Action dated March 22, 1991 in connection with the prosecution of U.S. Patent Application No. 07/531,953, filed June 1, 1990.
23. Cited in an Information Disclosure Statement Under 37 C.F.R. 1.99 filed September 23, 1991 in connection with the prosecution of U.S. Patent Application No. 07/531,953, filed June 1, 1990.
24. Cited in an Office Action dated October 3, 1991 in connection with the prosecution of U.S. Patent Application No. 07/532,461, filed May 31, 1990.
25. Cited in an Office Action dated January 3, 1992 in connection with the prosecution of U.S. Patent Application No. 07/520,682, filed May 8, 1990.
26. An English abstract of this document is included.

* * * * *

Form PTO-1449 U.S. Department of Commerce (REV. 8-83) Patent and Trademark Office INFORMATION DISCLOSURE CITATION (use several sheets if necessary)	Atty. Docket No. Enz-5 (D6)(C1)	Serial No. 08/046,004
	Applicants: Dean L. Engelhardt et al.	
	Filed: April 9, 1993	Group: 1807

U.S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER							DATE	NAME	CLASS	SUB CLASS	FILING DATE IF APPRO- PRIATE
		2	5	5	2	2	3	04/17/81	Ward et al.			
	4	7	0	7	4	4	0	11/17/87	Stavrianopoulos			
	4	0	3	8	4	8	0	07/26/77	Robins et al.			
	4	2	1	3	8	9	3	07/22/80	Carrico et al.			
	4	2	5	5	5	6	6	03/10/81	Carrico et al.			
	4	3	7	8	4	5	8	03/29/83	Gohlke et al.			
	4	4	4	3	5	9	4	04/17/84	Buckmann			
	4	4	6	0	7	7	2	07/17/84	Benovic et al.			
	3	9	3	1	3	9	7	01/06/76	Harnden			
	4	1	2	4	7	0	2	11/07/78	Lampson et al.			
	4	3	1	3	9	3	8	02/02/82	Arimura et al.			

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER							DATE	COUNTRY	CLASS	SUB CLASS	TRANS- LATION	
													YES	NO
	5	3	1	3	3	2	8	3	11/34	Japan				
	2	0	3	6	0	2	9	A	06/25/80	UK				
	5	7	1	1	9	9	9		1/82	Japan				
	6	0	9	6	6	1	0		5/85	Japan				
	0	0	6	3	8	7	9	B1	11/23/82	EP				

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	4	7	1	1	9	5	5	12/08/87	Ward et al.			
	4	3	5	8	5	3	5	11/82	Falkow et al.			
	5	2	6	0	4	3	3	11/09/93	Engelhardt et al.			
	4	5	8	1	3	3	3	04/08/86	Kourilsky et al.			
	4	6	0	5	7	3	5	08/12/86	Miyoshi et al.			
	9	7	0	8	9	3	5	11/24/87	Suhadulnik et al.			
	4	8	8	0	9	1	8	11/24/89	Rapaport			
	4	8	2	8	9	7	9	5/9/89	Klevan et al.			
	4	8	3	3	2	5	1	05/23/89	Musso et al.			
	3	9	6	0	8	4	0	06/01/76	Secrist, III et al.			
	4	2	3	0	7	9	7	10/28/80	Boguslaski et al.			

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		DOCUMENT NUMBER							DATE	COUNTRY	CLASS	SUB CLASS	TRANS- LATION	
													YES	NO
	2	0	4	0	9	4	3		09/03/80	UK				
	2	0	1	9	4	0	8	A	10/31/79	UK				
	6	0	1	6	9	4	9	5	09/85	JP				
	0	1	6	9	7	8	7	A1	1/29/86	EP				
	8	6	0	2	9	2	9		5/22/86	PCT				

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Bhat, Syn. Proc. in Nucleic Acid Chem., Vol. I., p. 521 (1968)
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	4	2	6	0	7	3	7	04/07/81	Scherberg			
	4	3	1	0	6	6	2	01/12/82	Crea			

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER							DATE	COUNTRY	CLASS	SUB CLASS	TRANS- LATION	
													YES	NO
		5	7	4	2	6	3	2	3/86	JP				
		6	1	1	0	3	8	2	4	5/86	JP			
		0	0	2	7	6	3	1	B1	05/05/82	EP			
		0	2	2	5	8	0	7	A2	06/16/87	EP			
WO		8	3	0	2	2	7	6		07/07/83	PCT			

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	Bleackley et al., "The preparation of 5-cyanouracil and 5-cyano-2'-deoxyuridine from the corresponding 5-iodo derivative and cuprous cyanide," <u>Nucl. Acids Res.</u> , 2(5):683-690 (1975)
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														YES	NO
WO		8	3	0	2	2	7	7	07/07/83	PCT					
		A	6	5	9	5	7	3	04/30/79	SU					
	0	0	6	1	7	6	2	A2	10/06/82	EP					
	0	0	6	1	7	6	0	A1	10/06/82	EP					
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OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

Miller, J., "Experiment 52, Assay of the lac Repressor by Binding to Operator," <u>Experiments in Molecular Genetics</u> , Cold Spring Harbor Laboratory, pp. 367-370 (1972)

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		DOCUMENT NUMBER								DATE	COUNTRY	CLASS	SUB CLASS	TRANSLATION	
														YES	NO
DE	A	2	5	0	7	9	0	1			DE				
DE	A	1	8	1	4	1	3	4			DE				
DE	A	1	6	1	7	8	8	6			DE				

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

Monod et al., "On the Nature of Allosteric Transitions: A Plausible Model," <u>J. Mol. Biol.</u> , 12:88-118 (1965)
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	Caruthers, Second Annual Congress for Recombinant DNA Research, Los Angeles, CA (1982)
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	DOCUMENT NUMBER								DATE	COUNTRY	CLASS	SUB CLASS	TRANS- LATION	
													YES	NO

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	Siebenlist et al., "Contacts between Escherichia Coli RNA polymerase and an early promoter of
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Form PTO-1449 U.S. Department of Commerce (REV. 8-83) Patent and Trademark Office INFORMATION DISCLOSURE CITATION (use several sheets if necessary)	Atty. Docket No. Enz-5 (D6)(C1)	Serial No. 08/046,004
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FOREIGN PATENT DOCUMENTS

	DOCUMENT NUMBER								DATE	COUNTRY	CLASS	SUB CLASS	TRANS- LATION	
													YES	NO

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Hoffman et al., "Iminobiotin Affinity Columns and Their Application to Retrieval of

Sheet 9 of 12

Form PTO-1449 U.S. Department of Commerce (REV. 8-83) Patent and Trademark Office INFORMATION DISCLOSURE CITATION (use several sheets if necessary)	Atty. Docket No. Enz-5 (D6)(C1)	Serial No. 08/046,004
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	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB CLASS	TRANS- LATION	
						YES	NO

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FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER								DATE	COUNTRY	CLASS	SUB CLASS	TRANS- LATION	
														YES	NO

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	Clochet, P. et al., "Trace analysis of barium in water by means of cation resin-loaded paper and "
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Sheet 11 of 12

Form PTO-1449 U.S. Department of Commerce (REV. 8-83) Patent and Trademark Office INFORMATION DISCLOSURE CITATION (use several sheets if necessary)	Atty. Docket No. Enz-5 (D6)(C1)	Serial No. 08/046,004
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FOREIGN PATENT DOCUMENTS

	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB CLASS	TRANS- LATION	
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OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

Trouet et al., "Targeting of antitumor and antiprotozoal drugs by covalent linkage to protein

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Form PTO-1449 U.S. Department of Commerce (REV. 8-83) Patent and Trademark Office INFORMATION DISCLOSURE CITATION (use several sheets if necessary)	Atty. Docket No. Enz-5 (D6)(C1)	Serial No. 08/046,004
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FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB CLASS	TRANSLATION	
							YES	NO

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

Zhenodarova et al., "Spin-labeled Derivatives of Oligoribonucleotides as Spin Probes for Studying the Mechanism of the Effect of Enzymes" <i>Chemical Abstracts</i> Vol. 91, 1979
